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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/748,642	12/22/2000	Thomas B. Albrecht	026.00041	4973

7590 10/23/2002

Braman & Rogalskyj, LLP
P.O. Box 352
Canandaigua, NY 14424-0352

EXAMINER
LACOURCIERE, KAREN A

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/23/2002

8

Please find below and/or attached an Office communication concerning this application or proceeding.

FILE COPY

Office Action Summary	Application No.	Applicant(s)	
	09/748,642	ALBRECHT ET AL.	
	Examiner	Art Unit	
	Karen A. Lacourciere	1635	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *2-4 and 10-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-9 and 13-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12-22-00* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II in Paper No. 7 is acknowledged. The traversal is on the ground(s) that the search of both Groups I and II would not be a burden and the inventions of Group I and II are not distinct. This is not found persuasive because the search of the inventions of Group I and II would require separate searches and, therefore, would present a burden, and is reflected in the different classification of the inventions. Further, although there are generic claims that encompass the subject matter of Group I and Group II, Applicant has not provided any evidence showing these inventions are obvious variants, nor has Applicant clearly admitted on the record that this is the case. Should Applicant provide such evidence or statement, in either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

The requirement is still deemed proper and is therefore made FINAL.

Claims 2-4 and10-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1, 5, 6 and 7 are rejected under 35 U.S.C. 102(e) as being anticipated by Potter et al. (US Patent No. 6,294,518).

Potter et al. discloses methods wherein calpastat, a calpain inhibitor, is administered to an HIV infected human promonocytic cell line and HIV-1 viral production is inhibited (see for example column 13, example 5). Therefore, Potter et al. anticipates claims 1, 5, 6 and 7.

Claims 1, 5, 9, 13 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Gordon et al. (reference 5 on PTO form 1449, filed July 19, 2002).

Gordon et al. disclose methods wherein an inhibitor of HIV cellular protease is administered to cells in a subject and the replication of HIV virus is inhibited and a treatment effect for HIV is obtained.

Therefore, Gordon et al. anticipates claims 1, 5, 9, 13 and 17.

Claims 1, 5, 9, 13, 17 and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Roizman et al.

Roizman et al. disclose methods of inhibiting the replication of a virus, including herpes simplex virus and human cytomegalovirus, by administering an inhibitor of a viral protease.

Therefore, claims 1, 5, 9, 13, 17 and 18 are anticipated by Roizman et al.

Claims 1, 5-9 and 13-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Henkart et al. (reference 2 on PTO form 1449, filed July 19, 2002).

Henkart et al. disclose methods wherein a calpain inhibitor is administered to HIV infected cells, including wherein the calpain inhibitor is E-64 (see for example column 3) and Z-Leu-Leu-H (see for example column 7). Henkart et al. disclose administering these inhibitors to an individual or ex vivo to cells of an individual for treatment of HIV infection.

Therefore, Henkart et al. anticipates claims 1, 5-9, and 13-17.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-9 and 13-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of inhibiting viral replication

using protease inhibitors disclosed in the art, does not reasonably provide enablement for generally inhibiting viral replication in any cell in any setting using generally any protease inhibitor, nor does it enable the skilled artisan to prevent infection by inhibiting a cellular protease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

Claims 1, 5-9 and 13-18 are drawn broadly to inhibiting the replication of generally any virus and treating or preventing generally any viral infection in an individual by inhibiting the activity of a cellular protease.

The methods of claims 9 and 13-18 are particularly drawn to methods of preventing infection of a virus by inhibiting the activity of a cellular protease. Cellular protease may be a host cell protease or a viral protease produced in the host cell, however, the limitation "cellular" would require that the protease be in the cell. Therefore, in order for the inhibitor of the cellular protease to be active in the claimed method, it would require that the virus be in the cell, post infection, therefore, it does not seem possible to inhibit infection of a virus by the claimed methods.

The specification discloses methods wherein the calpain inhibitors E64d and Z-Leu-Leu-H are administered to HCMV infected cells in vitro, which results in an inhibition of the degradation of $p21^{cip1}$ in those cells relative to untreated HCMV infected cells. The specification does not provide any evidence that HCMV replication is inhibited by E64d or Z-Leu-Leu-H, in vivo or in vitro, nor does it provide any evidence that administering E64d or Z-Leu-Leu-H to a subject treats a viral infection in said subject. The prior art discloses methods which are enabled, that fall within the scope of the claimed methods (see for example, the rejection of record under 35 USC 102 as anticipated by Gordon et al.), however, such methods are a very small scope of the claimed methods, and would not enable the full scope of methods claimed. The prior art also discloses methods wherein protease inhibitors are administered to treat viral infections, and comprise the steps of the claimed methods and would inherently have any treatment effect as the claimed methods, however, these methods are only enabled to the same extent as the claimed methods and do not provide the guidance required to practice the methods over the full scope claimed.

At the time of the instant invention, and even to date, methods of treatment for viral infections were unpredictable, and the life cycle of many viruses were unknown or not well defined. The art of the field of viral infections did not provide sufficient information to know what viruses require cellular proteases for replication, or what particular proteases are used by a particular virus. The specification does not provide guidance by which the skilled artisan would know what protease to inhibit for particular viral infections, or replication of a particular virus. Even for the specifically claimed

embodiment of calpain inhibitors, the art demonstrates that inhibition of calpain does not necessarily cause inhibition of replication. For example, Debaisi et al. (reference 8 on PTO form 1449, filed July 19, 2002) demonstrates that calpain inhibitors act independent of reovirus replication (see abstract, for example). Additionally, Debaisi et al. disclose that calpain may be involved in many physiological roles in a viral infected cell, but that further research would be required before a potential therapeutic intervention can be developed (see for example, p 699). The instant specification does not provide sufficient information regarding the very broad scope of viral infections encompassed by the claims, such that the skilled artisan would be able to practice the full scope claimed. In order to practice the scope of the claimed methods, one skilled in the art would need to undergo undue trial and error experimentation to determine what viruses can be treated using a particular protease inhibitor and how to treat such a viral infection in an individual. Given the complex nature of viral infections, and the difficulty in determining effective treatments, even through this undue trial and error experimentation, the skilled artisan may never be successful.

Therefore, at the time of the instant invention, one skilled in the art would not have been able to practice the claimed invention over the full scope claimed without undue trial and error experimentation.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Lacourciere whose telephone number is (703) 308-7523. The examiner can normally be reached on Monday-Friday 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-1935 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Karen A. Lacourciere
October 21, 2002